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-- PATENT APPLICATION
-- Attorney Docket No. 25,835,11
GROUP 1800

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: M. L. Collins, et al.
Serial No.: 08/238,080
Filing Date: May 3, 1994
Title: TARGET AND BACKGROUND CAPTURE
METHODS WITH AMPLIFICATION FOR
AFFINITY ASSAYS
Art Unit: 1807
Examiner: Dianne Rees, Ph.D.

CERTIFICATE OF MAILING & FACSIMILE RESPONSE

I hereby certify that this correspondence is being sent via facsimile to: Dianne Rees, at facsimile number (703) 305-3014, and is being deposited with the United States Postal Service as first class mail, postage prepaid, in an envelope addressed to: The Commissioner of Patents and Trademarks, Washington, D.C. 20231, on the date shown below.

LESLIE B. HENSON

(Printed Name)

Leslie B. Henson
(Signature)

July 9, 1997

(Date of Deposit)

TRANSMITTAL OF DECLARATION
OF DAVID H. PERSING, M.D., PH.D.

The Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Applicants submit herewith the Declaration of Dr. David H. Persing pursuant to 37 CFR §1.132 for purposes of traversing the Examiner's rejections of pending claims 25-50. Applicants submit that Dr. Persing's Declaration provides additional compelling evidence of the patentability of Applicants' claimed inventions.

In particular, Applicants have previously contended that practitioners in the nucleic acid hybridization and amplification arts at the time the invention was made were deterred from using nucleic acid hybridization to separate target from sample prior to amplification because of their concern over the loss of target prior to amplification resulting from the incomplete binding efficiency between hybridization probe and target. While the Examiner has acknowledged the legitimacy of Applicants' contention, the Examiner remains unpersuaded as to the patentability of Applicants' claimed inventions. The Examiner contends that Applicants'

submission is balanced by the consideration that practitioners would have been motivated to use hybridization to separate target from sample prior to amplification because doing so would provide a more specific target for amplification. (See the Examiner's Interview Summary for the Interview dated April 7, 1997) Applicants submit Dr. Persing's Declaration to overcome the Examiner's contention. Applicants submit Dr. Persing is an expert in the field of nucleic acid hybridization assays utilizing amplification methods such as PCR. Dr. Persing has been a practitioner in this field since about 1985 or before the invention was made. He is knowledgeable as to the practices and concerns of practitioners at that time. Dr. Persing's Declaration is also submitted to demonstrate that Applicants' invention provides advantages unanticipated by the art at the time the invention was made. His testimony is supported by published technical references.

Applicants submit Dr. Persing's testimony overcomes the Examiner's contentions that those skilled in the art would have been motivated to choose from the various available techniques and arrive at Applicants' intention. As Dr. Persing states, those practicing in this art at the time the invention was made were, in fact, concerned with the incomplete binding efficiencies of probe to target and the expected resulting loss of target, and were deterred from performing hybridization and separation prior to amplification as a result. (Dr. Persing's testimony is supported by the reference text **Diagnostic Molecular Microbiology PRINCIPALS AND APPLICATIONS**, attached as Exhibit 3 to his Declaration.) As Dr. Persing also states, this deterrence was reinforced by the general teachings of PCR practitioners that PCR was highly specific and could be made to selectively amplify a desired target in an otherwise complex sample so that there was no need to risk losing target by hybridization and separation prior to amplification. Contrary to the Examiner's contentions, those practicing in this art were motivated against finding Applicants' invention rather than toward Applicants' invention.

Finally, Dr. Persing's Declaration demonstrates that Applicants' invention provides an additional advantage that was not perceived at the time the invention was made. This is the removal of amplification inhibitors from the amplification medium prior to the actual amplification of the target nucleic acids, which is also discussed in the recently submitted Mangiapan article. (See Transmittal of Art References filed April 17, 1997) Thus, in addition to enabling more specific

target amplification, Applicants' invention enables the amplification to proceed more efficiently than would have been expected at the time the invention was made.

Applicants submit that the Examiner has, with the benefit of hindsight, oversimplified the difficulties perceived by those skilled in this art at the time the invention was made. (The Examiner has suggested, for example, that the general teachings of the art at the time of the invention and thereafter were of the "quick and dirty" variety. (See the Examiner's Interview Summary for the Interview dated March 26, 1997)) To the contrary, however, and as demonstrated by Dr. Persing's Declaration, the practitioners in this field perceived real and substantial deterrents against Applicants' invention at the time it was made. Applicants submit the invention represents a significant advance for those interested in the selective amplification of specific nucleic acid targets.

Since a Notice of Appeal has been filed, Applicants suppose that submission of the Persing Declaration must be accompanied by a showing of good and sufficient reasons why it was not presented earlier. (See 37 CFR §1.195) Applicants submit the Persing Declaration includes statements that could not have been presented earlier. Applicants were not aware of the teachings from **Diagnostic Molecular Microbiology** and the Mangiapan article, which are cited and discussed in the Declaration until only recently. Thus, Applicants were not able to present Dr. Persing's Declaration earlier.

Applicants submit herewith an unsigned Declaration of Dr. Persing. Dr. Persing's signature will be obtained shortly and the executed Declaration will be submitted at that time. Applicants again wish to express their gratitude to the Examiner for the consideration extended by the Examiner to Applicants' representative.

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Applicants submit that all claims are in condition for allowance, which action is earnestly solicited.

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Respectfully submitted,
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